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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,491	02/25/2004	David R. Guyer	EYE-010CON	3137

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EXAMINER	
CHONG, KIMBERLY	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 03/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/786,491	GUYER, DAVID R.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☒ Claim(s) *4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/15/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 02/27/2006 is acknowledged.

Status of the Application

Claims 1-20 are pending and currently under examination.

Claim Objections

Claim 4 is objected to as reciting non-elected subject matter. Claim 4 should be rewritten deleting any non-elected subject matter.

Priority

Claims 16 and 20 of the instant application are accorded the priority date of 02/25/2004, the filing date of the instant application. The instant application does not receive the benefit of the earlier filing date of the prior applications 10/291,091 and 60/332,304 because the claims are not supported by the specifications of the Provisional Applications and thus not supported by 35 U.S.C. § 112 first paragraph.

The claims are drawn to a method for treating an ocular neovascular disease in a patient comprising administering an aptamer comprising pegaptanib sodium. The prior applications disclose a method for treating an ocular neovascular disease in a patient comprising administering an aptamer targeted to VEGF. However, the prior applications do not disclose an aptamer comprising pegaptanib sodium.

If Applicant believes the prior applications provide support then applicant must point, with particularity, to where such support can be found in the specification of the prior applications.

Therefore, the priority date granted to claims 16 and 20 is 02/22/2004.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-16 and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drolet et al. (Pharmaceutical Research 2000) in view Kaplan et al. (U.S. Patent No. 5,342,348) and evidenced by Vinores, S. (Curr Opin Mol Ther. 2003).

The instant claims are drawn to a method of treating an ocular neovascular disease in a patient comprising administering an anti-VEGF agent, i.e. an aptamer, wherein the aptamer is provided in a controlled release formulation comprising a biocompatible or biodegradable polymer, wherein the neovascular disease is age-related macular degeneration or proliferative diabetic retinopathy, wherein the anti-VEGF aptamer comprises a nucleic ligand to VEGF wherein the VEGF nucleic ligand comprises a ribonucleic acid or a deoxyribonucleic acid, 2'-F modified nucleotides, a polyethylene glycol or 2'-O-methyl modified nucleotides.

Drolet et al. teach a method of treating an ocular neovascular disease comprising administering an anti-VEGF aptamer (NX1838) comprising a polyethylene glycol (see first

paragraph page 1503). Drolet et al. teach NX1838 is currently used to treated age-related macular degeneration (see column 2 page 1503). Drolet et al. teach said anti-VEGF aptamer comprises 2'-F modified nucleotides and 2'-O-methyl modified nucleotides to reduce nuclease susceptibility (see page 1503). It is noted that the aptamer taught by Drolet et al., NX-1838 comprises pegaptanib and is also called EYE-001, Macugen and pegaptanib octasodium (see Vinores, S. Technology evaluation: pegaptanib, Eyetech/Pfizer 2003, page 673 and 674). Drolet et al. does not teach a method of delivering the aptamer and a biodegradable polymer in a controlled release formulation .

Kaplan et al. teach a method of delivery of compounds in a controlled release formulation (see column 4, lines 41-60). Kaplan et al. teach a formulation comprising a biocompatible polymer wherein the polymer is a lactide polymer (see column 6) and further teach the formulation is suitable for delivery of an aptamer (see column 7, lines 53-68).

It would have been obvious to one of ordinary skill in the art to delivery the anti-VEGF aptamer taught by Drolet et al. using a controlled release formulation comprising a biocompatible polymer, as taught by Kaplan et al.

One would have been motivated to deliver the anti-VEGF aptamer in a controlled release biodegradable formulation because Kaplan et al. teach it would be desirable to provide methods that can provide medication to targeted regions and provide long-term delivery of medications to targeted regions (see column 2, lines 6-19). Further, biodegradable polymers, as taught by Kaplan et al., are easily constructed and well known to one of skill in the art (see column 6, lines 38-53).

Finally, one would have a reasonable expectation of success given that Kaplan et al. teach the steps of delivery of a biodegradable polymer to vessels and Drolet et al. teach an efficient method to deliver an anti-VEGF aptamer to treat an ocular neovascular disease and the anti-VEGF aptamer taught by Drolet et al. because is target specific and specifically inhibits VEGF mediated cellular responses as well as it is safe when injected into the vitreous humor of an animal and has an increased half life.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. (US 2002/0040015) in view of Ruckman et al. (J Biol. Chem. 1998, Vol. 273: 20556-20567) and Kaplan et al. (U.S. Patent No. 5,342,348) evidenced by Vinores, S. (Curr Opin Mol Ther. 2003).

The instant claims are drawn to a method of treating an ocular neovascular disease in a patient comprising administering an anti-VEGF agent, i.e. an aptamer, wherein the aptamer is provided in a controlled release formulation comprising a biocompatible or biodegradable polymer, wherein the neovascular disease is age-related macular degeneration or proliferative diabetic retinopathy, wherein the anti-VEGF aptamer comprises a nucleic ligand to VEGF wherein the VEGF nucleic ligand comprises a ribonucleic acid or a deoxyribonucleic acid, 2'-F modified nucleotides, a polyethylene glycol or 2'-O-methyl modified nucleotides, wherein the aptamer comprises pegaptanib sodium and wherein the anti-VEGF aptamer is delivered to the eye by transcleral diffusion.

Miller et al. teach a method of treating ocular neovascular disease in a patient comprising administering a nucleotide that binds VEGF (see paragraph 0012-0014) for such conditions such as neovascular age-related macular degeneration (see paragraph 0010). Miller et al. further teach the nucleic acid that binds VEGF is modified to be more resistant to nuclease degradation (see paragraph 0057) and is administered by injection wherein administration comprises introducing a device into the eye by transcleral diffusion or into the vitreous humor of the eye (see paragraph 0060). Miller et al. teach the anti-VEGF aptamer may be delivered using a continuous release biodegradable device immobilized in the eye for transscleral delivery (see paragraph 0060). Miller et al. does teach an anti-VEGF aptamer comprising 2'-F or 2'-O-methyl modified nucleotides and does not teach a controlled release formulation comprising a biocompatible or biodegradable polymer as recited in claim 1.

Ruckman et al. teach an anti-VEGF aptamer comprising a ribonucleic acid or a deoxyribonucleic acid wherein the inhibition of VEGF is implicated in the treatment of macular degeneration or diabetic retinopathy (see page 20556, column 2). Ruckman et al. further teach an anti-VEGF aptamer comprising a 2'-F modification nucleotides, polyethylene glycol, 2'-O-methyl modified nucleotides and modified with a moiety that decreases the activity of endonucleases and further teach the utility of aptamers as therapeutic or diagnostic agents is considerably enhanced by chemical modifications (see pages 20556, paragraph 2). It is noted that the aptamer taught by Ruckman et al., VEGF-165 comprises pegaptanib and is also called EYE-001, NX-1838, Macugen and pegaptanib octasodium (see Vinores, S. Technology evaluation: pegaptanib, Eyetech/Pfizer 2003, page 673 and 674).

Kaplan et al. teach a method of delivery of compounds in a controlled release formulation (see column 4, lines 41-60). Kaplan et al. teach a formulation comprising a biocompatible polymer wherein the polymer is a lactide polymer (see column 6) and further teach the formulation is suitable for delivery of an aptamer (see column 7, lines 53-68).

It would have been obvious to one of ordinary skill in the art to incorporate the modifications, as taught by Ruckman et al. into the anti-VEGF aptamer taught by Miller et al. Further, it would have been obvious to one of ordinary skill in the art to delivery the anti-VEGF aptamer taught by Miller et al. using a controlled release formulation comprising a biocompatible polymer, as taught by Kaplan et al.

One would have been motivated to incorporate the modifications into the oligonucleotides taught by Miller et al because Ruckman et al. teach aptamers comprising modified nucleotides have increased stability and target affinity (see page 20557) and teach aid aptamers are very specific ligands that interfere with protein-protein interactions and prevent VEGF from binding to its receptor. Additionally, One would have been motivated to deliver the anti-VEGF aptamer in a controlled release biodegradable formulation because Kaplan et al. teach it would be desirable to provide methods that can provide medication to targeted regions and provide long-term delivery of medications to targeted regions (see column 2, lines 6-19). Further, biodegradable polymers, as taught by Kaplan et al., are easily constructed and well known to one of skill in the art (see column 6, lines 38-53).

Finally, one would have a reasonable expectation of success given that Miller et al. teach method to deliver an anti-VEGF aptamer along with photodynamic therapy and Ruckman et al. teach a method of making modified anti-VEGF aptamers targeted to VEGF.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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1635

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